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08/819669

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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/819,669	03/17/97	BOON	T LUD-5253.5-D

HM12/1227

NORMAN D HANSON
FULBRIGHT & JAWORSKI L.L.P.
666 FIFTH AVENUE
NEW YORK NY 10103

EXAMINER	
GAMBEL, P	
ART UNIT	**PAPER NUMBER**
1644	27

DATE MAILED: 12/27/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 11/3/98; 2/5/99; 6/7/99; 8/27/99

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☐ Claim(s) _____ is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☐ Claim(s) _____ is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☑ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892 ☑ NOTICE TO COMPLY WITH SEQUENCE RULES
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☑ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

* U.S. GPO: 1998-404-498/405

DETAILED ACTION

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1644.

2. Claims 1-172, 175, 177, 178 and 180 have been canceled previously.
Claims 173, 174, 176, 179, 181 and 182 are pending.

3. No Information Disclosure Statements appear in the instant application.

Application is reminded that IDS's as well as affidavits and declarations, such as those under 37 C.F.R. § 1.131 and 37 C.F.R. § 1.132, filed during prosecution of the parent application do not automatically become a part of this application. Where it is desired to rely on an earlier filed IDS or affidavit; the applicant should make the remarks of record in the later application and include a copy of the original IDS or affidavit filed in the parent application.

4. Applicant's comments concerning the discussion and agreement in a telephone interview, held on 12/22/98, with Richard Schwartz, Christina Chan and Thomas Cunningham are acknowledged.

As indicated previously to applicant in an interview, held on 9/7/99; the current examiner cannot determine what was discussed or agreed upon other than what is in the file application.

The examiner apologizes for any misunderstanding or inconvenience to applicant.

This Office Action addresses the current claimed invention and takes into account the prosecution history set forth in the instant file application.

5. Applicant's amendment, filed 9/27/99 (Paper No. 24), is acknowledged.
Applicant's sequence submission is acknowledged and appears to be in compliance with the sequence rules, except for the following.

A) There does not appear to be SEQ ID NOS. for the sequences set forth on pages 49-50 of the instant specification. It is acknowledged that applicant has amended the claims to indicate such sequences are complements of other SEQ ID NOS. However; given that these nucleotide sequences embrace ten or more bases; then applicant must comply with the Sequence Rules.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

B) With respect to correcting SEQ ID NOS: 7 and 8; see the New Matter rejection below.

6. Applicant should amend the first line of the specification to update the status of the priority documents. For example, USSN /07/764,365 is now abandoned.

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

8. The Abstract of the Disclosure is objected to because it does not adequately describe the claimed invention. Correction is required. See MPEP 608.01(b).

9. Formal drawings, filed 3/17/97, comply with 37 CFR 1.84.

However, the Brief Description of the Drawings should indicate that Figure panels are separately labeled and individually described (e.g. Figure 1A, Figure 1B) and should indicate the appropriate SEQ ID NOS. (e.g. Figure 9).

10. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

The page numbers of specification must be numbered consecutively. For example, page 13 follows page 34 in the specification as filed.

For example, "BALB/c" is the proper designation of this mouse strain (see pages 27-28).

Applicant is required to identify the nucleotide and amino acid sequences in the specification with SEQ. ID NOS.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

11. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

The reference to USSN 07/764,364 in the oath appears in error, as this application issued as U.S. Patent No. 5,327,252 directed to a print apparatus.

Application Number 764,364 has the last "4" crossed out and "PCT/US92/04354 / 22May 1992" has been crossed out.

12. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. New Matter with respect to SEQ ID NOS: 7 and 8.

The amendment filed 7/8/98 (Paper No. 11) as well as previous submissions of the "corrected SEQ ID NOS; 7/8 are objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: SEQ ID NOS 7/8 for the reasons indicated below.

Applicant is required to cancel the new matter in the reply to this Office action.

Claims 176 and 182 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: the corrected sequence of SEQ ID NO: 8.

Upon a review of the instant application, the following is noted.

See Applicant's amendment, filed 7/8/98 (Paper No. 11).

The nucleotide sequences at SEQ ID NO:7 and SEQ ID NO: 8 have been modified. These changes involve one nucleotide at the position following base 1377 in SEQ ID NO: 7 and one following nucleotide 4633 in SEQ ID NO: 8.

Applicant asserts that the changes present specific sequences taken from specific clones, hence the sequence of these clones is inherent and relate to the type of correction which is permissible and does not introduce new matter

Applicant's arguments or record in conjunction with the Boon/van der Bruggen/van den Eynde declaration under 37 C.F.R. § 1.132, filed 7/9/98 (Paper No. 12), have been fully considered but are not found convincing with respect to new matter.

The inventors' declaration was submitted to correct errors SEQ ID NOS:7/8. Applicant set forth the following;

Examples 20/21 in the specification as filed discloses the isolation of a 1.8 kilobase and a 2.4 kilobase genomic DNA clones

Applicant screened cDNA libraries, identifying a 1.3 kilobase cDNA, sequenced it to obtain a deduced sequence (July 4, 1991); however these sequences were not complete and were not included in the patent application.

Applicant sequenced the 2.4 kilobase genomic clone, which was determined to be in error.

Applicant used the 1.3 kilobase cDNA clone as a probe to identify a 1.7 kb cDNA molecule, which was sequenced (July 4, 1991), which was determined to be in error as well.

Applicant relied upon the sequence of the 1.7 kb cDNA and 2.4 kb gDNA clones in the instant application.

Then, applicant prepared a second cDNA library using the same source of mRNA used to isolate the 1.7 kb clone discussed above and identified a cDNA clone which was 10 base pairs longer than the 1.7 kb fragment.

This 1.7 kb plus 10 base pair cDNA was transferred to another vector and then sequenced by scientific collaborators; wherein a base pair difference was determined from the original sequence information (June 1993)

Within 48 hours of receiving this information, applicant resequenced the 1.7 kb plus 10 base pair cDNA, which was in agreement with the scientific collaborators.

Applicant attributed this change in sequence information to the well known phenomenon of band compression

Applicant resequenced the 1.3 kb cDNA molecule and determined that it was identical to the 1.7 kb plus 10 base pair cDNA, which differed from the 1.7 kb cDNA molecule.

It is noted that the patent application relied upon the sequence information from the 1.7 kb cDNA molecule.

Applicant corrected the sequence in Genbank database late in 1993 and did not consider any patent matters in terms of correction.

Applicant states that the error arose without any deceptive intent.

In contrast to applicant's assertions or new matter; the following is noted.

With respect to the specification as filed, Example 20 discloses a 2.4 kb fragment from MZ2-MEL, identified as SEQ ID NO: 7 (sce pages 37-39) and Example 21 discloses that the 2.4 kb fragment was used as a probe to identify a 1.8 kb fragment (see page 40).

Therefore, the specification as filed discloses a 2.4 kb fragment and a 1.8 kb fragment and not a 1.7 kb and or a 1.3 kb fragment, as relied upon by applicant. The specification as filed does not appear to disclose either the 1.7 kb or the 1.3 kb fragment nor the 1.7 kb plus 10 base pair cDNA set forth in applicant's Declaration.

Further, applicant relies upon obtaining a second cDNA library to obtain appropriate clones and sequence information, wherein neither the second library, nor subsequent clones were disclosed in the specification as filed.

There is unpredictability that a second cDNA library relied upon by applicant to change sequences would be necessarily the same as the first cDNA library disclosed in the specification as filed. Further there is insufficient objective evidence that the sequence now relied upon by applicant was based upon either the 2.4 kb fragment and a 1.8 kb fragment; which were disclosed in the specification as filed. Also, it was well known that enzymes used in making a cDNA from mRNA library are prone to error incorporating the wrong nucleotides (see Richetti et al. EMBO J. 9: 1583 - 1593, 1990; see entire document, including Abstract). It is not clear that the difference of the missing nucleotide "C" is a result of a compression, as set forth by the declaration.

It is noted applicant appears to have a corrected a sequence or obtain a new sequence in 1993; but did not disclose either in the instant application USSN 08/819,669, filed 3/17/97, nor in the parent application USSN 08/142,368, filed 5/2/94 at the time of filing either application.

Therefore, a review of the instant application does not provide for sufficient information concerning either the SEQ ID NOS: 7/8 now disclosed and claimed nor does it provide for the materials now relied upon by applicant to correct said sequences (e.g. second library, distinct clones and nucleic acid molecules). Here, applicant does not rely upon the original starting materials disclosed (or deposited) in the specification as filed.

Also, see Ex parte Maizel 27 USPQ2d 1662 (BPAI 1992)

Here, applicant also is claiming generically tumor rejection antigen precursor encoded by nucleotide sequences that hybridize to SEQ ID NO:8; therefore the claims are not limited to specific sequence set forth either in the claims or in the instant disclosure.

Without an accurate written description of the nucleic acid, the skilled artisan cannot describe or envisage either the correct nucleic acid sequence, nor any nucleotide sequence that hybridizes thereto to describe a tumor rejection antigen precursor.

The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action
Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above.

14. Claims 176 and 182 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 176 and 182 are rejected in the recitation of "stringent conditions" because the metes and bounds of said conditions are not clearly defined. The term in clam is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 173, 174, 176, 179, 181 and 182 are rejected under 35 U.S.C. § 103(a) as being unpatentable over van den Eynde et al. (Int. J. Cancer 44: 634-640, 1989) in view of art known methods of isolating antigens of interest as taught by de Plaen et al (PNAS 85: 2274-2278, 1988) AND/OR Brown et al. (U.S. Patent No. 5,141,742) AND/OR Seed et al. (U.S. Patent No. 5,506,126) and in further evidence by Van der Bruggen et al. (Science 254: 1643-1647, 1991) and Traversari et al. (Immunogenetics 35: 145-152, 1992)

Van den Eynde et al. teach the presence and identification of human melanoma antigens recognized by cytotoxic T lymphocytes, including antigen E and its prospects for immunotherapy (see entire document).

Van der Bruggen et al. and Traversari et al. (see entire documents) both acknowledge that the information disclosed in the instant specification, including that related to the antigen associated with the 2.4 kb fragment disclosed in Example 20 of the specification and encompassed by the claimed invention is the same antigen as antigen E disclosed in Van den Eynde et al.

Van den Eynde et al differs from the claimed invention by not isolating the melanoma antigen encompassed by the claimed invention.

De Plaen et al. teach the same cloning of tumor antigens as disclosed Van den Eynde et al. (See References on page 640) as well on page 14 in Example 2 of the specification.

Brown et al. teach the isolation and cloning of melanoma antigens (see entire document).

Seed et al. teach the rapid immunoselection cloning method for cell surface antigens (see entire document).

Therefore, there were known means to isolate and to characterize cell surface or melanoma antigens or interest, including their use in composition formulations at the time the invention was made.

Therefore, given the identification of antigen E in the prior art and given various methods known to the skilled artisan to isolate as well as to clone cell surface of melanoma antigens of interest; the ordinary artisan would have been motivated to isolate said antigen E to determine its structural and functional properties in tumor-immune responses interactions, as routinely practiced at the time the invention was made. It would have been obvious to the ordinary artisan at the time the invention was made to isolate antigen E and to place into convenient compositions, including pharmaceutical compositions and vaccine formulations to elicit immune responses. For example, it was known at the time the invention was made that cell-mediated immunity was associated with tumor immunity. Further, it would have been obvious to generate antibodies to said tumor antigens, as tools in the isolation and detection of said antigens, as well as to generate immunotoxins, which was routinely practiced at the time the invention was made. It is noted that it is not necessary to clone antigen E to meet the claimed limitations, as it would have been obvious to ordinary artisan to isolate the antigen via conventional means, such as raising antibodies to said antigen E and to isolate it according to well known and practiced biochemical methods at the time the invention was made. The ordinary artisan would have isolated antigen E to determine its role in immune responses to tumors at the time the invention was made to place it into convenient formulations to generate responses to antigen E to determine structural and functional properties of said antigen E in tumor-immune responses interactions as routinely practiced at the time the invention was made.

Given that antigen E appears to the same antigen encompassed by the claimed invention, as evidenced by Van der Bruggen et al. and Traversari et al.; the SEQ ID NOS recited in the claimed would have been expected or intrinsic properties of isolated antigen E.

For examination purposes, the vaccine and composition claims read on compositions comprising the active ingredient of antigen 3, comprising SEQ ID NO: 26 and/or encoded by nucleotides hybridizing with SEQ ID NO: 8. The intended uses associated with "vaccine" or "with pharmaceutical appropriate ingredients" do not carry patentable weight per se over compositions comprising the active or essential ingredient of antigen 3.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Patent Examiner
Technology Center 1600
December 20, 1999

PHILLIP GAMBEL

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP ~~1800~~ 1640

09/819669

Application No.:_____

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☑ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☑ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☑ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☑ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☑ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☑ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE